REMARKS

I. The Pending Claims Are Not Anticipated By Chenchick et al., Bandaru et al., Nor By Wagner et al.

The Chenchick et al. Patent USP 6,087,102 Does Not Anticipate Each Element of The Claimed Invention.

The present application claims "providing a plurality of antibodies each having a signaling element when each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of the gene sequence".

This limitation is not found in the Chenchick reference. Furthermore, the identifying step of the present application:

> "Identifying differential gene expression between the at least two distinct biological conditions but correlating differences in the antibody binding reaction in the at least two samples with expression of the gene sequence identified with the number of the plurality of antibodies"

is not found in the Chenchick reference.

The Chenchick reference is a conventional example of a protein chip when the size of the member bound to the array assists in the identification of binding events. The so-called "probe" in the Chenchick disclosure is analogous to the binding antibodies of the present invention. However, as is made clear by the Chenchick specification, there is no correlation between the specific antibodies used in the reaction and the specific gene that may be subject to differential expression analysis. At column 10, lines 66 to column 11, line 2, the applicants notes that multiplex analysis requires the use of different probe molecules that are distinguishably labeled with different phlorophores. This approach demonstrates that the approach of Chenchick does not assign a specific gene expression event to a particular antibody used in the assay. The Chenchick specification also states that "the target expression level in the particular tissue being analyzed can be derived from the intensity of the detected signal. Chenchick also uses housekeeping genes to provide a control signal level to calibrate a signal provided by a particular probe. Thus, although Chenchick notes that the array described therein can be used for differential expression analysis, the differential expression is not detected by the binding reaction of a particular antibody that is linked to a particular gene. Further more, the "providing step" of the pending claims is not met by

Chenchick because the providing step that is cited by the Examiner does not meet the claimed element becsue there is no correspondeing element in Chenchick for the element of claim 14 recited as "wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence" as claimed.

Bandaru Does Not Disclose The Element of the Pending Claims Identified in the Previous Action.

> Bandaru does not disclose the method step of the present claims, specifically:
>
> providing a plurality of antibodies each having a signaling element wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence.

The Examiner is now citing to a different portion of Bandaru (column 51 rather than columns 4 and 60). In this embodiment, Bandaru still binds capture probes to the addresses of an array. This type of assay only yields information about a particular species (22109) that is the pre-determined target at the assay. As has been noted previously, the array and assays of Bandaru do not use the antibody binding events across the array for de novo expression profiling. In the present invention, gene expression information in a tissue sample is derived from the differential binding reactions of the "plurality of antibodies" reacting at two discrete sites of the array and when each is identified with an expression product of a gene sequence.

Wagner et al Does Not Anticipate the Presently Claimed Method

Referring to columns 6, 11, 12 and 37 of Wagner et al., Wagner et al. suffer from the same absence of disclosure as does Bandaru. Wagner et al. do not perform the method step of containing two tissue samples onto an array to obtain gene expression analysis. Wagner et al. distinguish their two samples using two identical arrays. Applicants specifically claim the contrary approach using two samples contained in discrete areas of a single array. Wagner et al. use protein capture agents as the member of the array. Please note that Wagner et al. specifically state:

> Typically, only one type of protein-capture agent is present on a single patch of the array. If more than one type of protein-capture agent is present on a single patch, all of the protein-capture agents of that patch must share a common binding partner. For instance, a patch may comprise a variety of polyclonal antibodies to the same antigen (although, potentially, the antibodies may bind different epitopes on that same antigen).

Using this approach, Wagner et al. cannot perform the method step of claim 14 quoted above wherein "providing a plurality of antibodies . . . wherein each member of the plurality of antibodies is identified as having specific binding affinity to an expression product of a gene sequence. . . ." Because this element is necessarily lacking from Wagner et al., Wagner et al. cannot anticipate under Section 102(a).

None of the above references meet the limitations of dependent claim 15 wherein antibodies are raised by in vivo immunization of a gene sequence. Applicants are specifically arguing the separate patentability of claim 15.

In light of the above, applicant requests favorable consideration and allowance of all of the newly presented claims. If the Examiner has any questions regarding the foregoing, or if the Examiner believes that an interview would facilitate the examination of this application, or if any additional information is required, the Examiner is invited to contact the undersigned at 949/567-6700, X 7740.

The Commissioner is authorized to charge a three month extension fee of $510.00 to ORRICK, HERRINGTON & SUTCLIFFE LLP's Deposit Account No. 150665. The Commissioner is also authorized to charge all applicable fees to ORRICK, HERRINGTON & SUTCLIFFE LLP's Deposit Account No. 150665 and to credit any overpayments to said Deposit Account No. 150665.

Respectfully submitted,
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